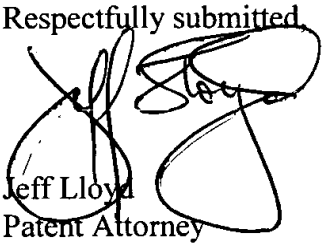
Remarks

This amendment is made to conform the application with the provisions of 37 CFR §§1.821 through 1.825. I hereby certify that no new material is being added by this submission.

Respectfully submitted,



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JL/srp
Attachments: Submission of Sequence Listing and Statement Under §1.821; New Sequence Listing pages 1-5; Petition and Fee for Extension of Time.

Marked-Up Version of Amended Specification

Please substitute the follow paragraphs:

Page 13, lines 15-22:

In formula II, R_1, R_2, R_3, and R_4, are each amino acid side chains that define a tetra-peptide sequence in which the tetra-peptide is covalently attached at the amino and carboxy termini of the tetra-peptide to a 3-aminomethyl-5-aminobenzamide linking group. In certain embodiments, for example PDGF-binding embodiments, the tetra-peptide sequence is selected from the group consisting of GDFD (SEQ ID NO. 1), GDDD (SEQ ID NO. 2), D-ADGD (SEQ ID NO. 3) in which the alanine is in the D conformation, other amino acids being in the L conformation), GDLD (SEQ ID NO. 4), GDAD (SEQ ID NO. 5), GDGY (SEQ ID NO. 6), ADGD (SEQ ID NO. 7), GDSD (SEQ ID NO. 8), GKGF (SEQ ID NO. 9), GKGK (SEQ ID NO. 10), GDND (SEQ ID NO. 11), PDGD (SEQ ID NO. 12), GDDG (SEQ ID NO. 13), GDDY (SEQ ID NO. 14), and functionally related derivatives thereof. In this embodiment, the preferred R group is *n*--butyl.

Page 19, line 18:

A novel series of protein surface binding agents are prepared that bind PDGF and disrupt its signaling function. The molecules are composed of a central calix[4] arene scaffold to which is attached four peptide loop domains (FIG. 1). The peptide loop component is based on a cyclic hexapeptide in which two residues are replaced by a 3-aminomethylbenzoate dipeptide mimetic containing a 5-amino substitutent for attachment to the scaffold. The resulting molecules (as shown in Table 1) contain a functionalized and vriable surface approximately 500Å^2 in area. Several peptide loop sequences are synthesized (Table 1) to provide molecular surfaces with negatively and positively charged as well as hydrophobic regions designed to bind to complementary areas on the target growth factor. To identify PDGF binding molecules from this library, a cell-based screening assay is developed with NIH 3T3 cells to detect molecules capable of blocking PDGF-BB-induced tyrosine

antophosphorylation of the PDGF receptor. The ability of the identified molecules to bind PDGF-BB and inhibit interaction with its receptor is then confirmed biochemically. Starved NIH 3T3 cells are pretreated for 5 min with the synthetic molecules prior to stimulation with PDGF for 10 min. The effects of the molecules on PDGF-stimulated receptor tyrosine phosphorylation are determined by the antiphosphotyrosine Western blotting as described in Table 1. GFB-111 is identified as one potential PDGF binder and as a potent (IC_{50}=250nM) inhibitor of PDGF-BB-stimulation of PDGF receptor tyrosine autophosphorylation (Table 1). GFB-111 has four-fold symmetry containing 4 identical peptide loops with negative and hydrophobic residues, GlyAspGlyTyr (GDGY) (SEQ ID NO. 6), that are designed to be complementary to the PDGF surface involved in binding to PDGFR. The area of PDGF-BB that binds PDGFR is composed primarily of positive and hydrophobic residues. Substitution of aspartic acid in the loop by positively charged lysine is poorly tolerated as can be seen by comparison of GFB-111 (GDGY) (SEQ ID NO. 6) (IC_{50}=250nM) to GFB-115 (GKGF) (SEQ ID NO. 9) (IC_{50}=50μM) and GFB-116 (GKGK) (SEQ ID NO. 10) (IC_{50}=40μM), indicating that negatively charged residues are important for the inhibitory activity of GFB-111. However, negatively charged residues along are not sufficient and the presence of an aromatic hydrophobic residue in the loop increases affinity as can be seen by comparison of GFB-111 (GDGY) SEQ ID NO. 6) with GFB-107 (GDGD) (SEQ ID NO. 16) (IC_{50}=2.5μM) as well as of GFB-122 (GDDY) SEQ ID NO. 14) (IC_{50}=1.7μM) with GFB-106 (GDDD) (SEQ ID NO. 2) (IC_{50}=8μM) (Table 1).

Page 20, Table 1:

Table 1. Inhibition of PDGF stimulated PDGFR Tyrosine Phosphorylation and Signaling in NIH 3T3 by GFBs.

Designation	Scaffold	R_1-R_4 sequence	(IC_{50}) Inhibition (μM)	
			PDGFR-Y-P	p42/Erk2
GFB-101	O4-Calix[A]	4-GFGD (SEQ ID NO. 15)	>500	>500

GFB-102	"	4-GDFD (SEQ ID NO. 1)	>500	500
GFB-103	"	4-GDGD (SEQ ID NO. 16)	>500	>500
GFB-104	O3-Calix[A]	4-GDGD (SEQ ID NO. 16)	>500	>500
GFB-105	But-Calix[A]	4-GDFD (SEQ ID NO. 1)	2.4	28
GFB-106	"	4-GDDD (SEQ ID NO. 2)	8	33
GFB-107	"	4-GDGD (SEQ ID NO. 16)	2.5	10
GFB-108	"	4-d-ADGD[1] (SEQ ID NO. 3)	9	57
GFB-109	"	4-GDLD (SEQ ID NO. 4)	7.5	15
GFB-110	"	4-GDAD (SEQ ID NO. 5)	1.7	7
GFB-111	"	4-GDGY (SEQ ID NO. 6)	0.25	2.6
GFB-112	"	4-ADGD (SEQ ID NO. 7)	29	26
GFB-113	"	4-GDSD (SEQ ID NO. 8)	2.8	30
GFB-114	"	(4-) 8-acid (See Figure 7)	>50	>50
GFB-115		4-GKGF (SEQ ID NO. 9)	>50	>50
GFB-116		4-GKGK (SEQ ID NO. 10)	40	28
GFB-117		4-GDND (SEQ ID NO. 11)	5.8	36
GFB-118		4-D-2-NalDGD[2] (SEQ ID NO. 17)	0.7	1.2
GFB-119		4-PDGD (SEQ ID NO. 12)	20	32
GFB-120	"	4-GDDG (SEQ ID NO. 13)	1.3	1.7
GFB-121	"	4-D-AbuDGD[3] (SEQ ID NO. 18)	5.6	8.5
GFB-122	"	4-GDDY (SEQ ID NO. 14)	1.7	19
GFB-123	"	1-GDDG (SEQ ID NO. 13)	>50	>50
GFB-124	"	See Figure 8	>50	>50

GFB-126	"	3 x GDDG (See Figure 9) (SEQ ID NO. 13)	1.9	4.6	
GFB-127	"	2 x GDDG (See Figure 9) (SEQ ID NO. 13)	32	>50	
GFB-128	"	DPM-2-GDGY (See Figure 10) (SEQ ID NO. 6)	26	>50	
GFB-129	"	DPM-2-GDDD (See Figure 10) (SEQ ID NO. 2)			
GFB-130	"	DPM-2-GDDY (See Figure 10) (SEQ ID NO. 14)			
GFB-131	"	DPM-2-GDDG (See Figure 10) (SEQ ID NO. 13)			
				p42	**p44**
GFB-132	But-Calix	3-GDGY (SEQ ID NO. 6)-1-GDDG (SEQ ID NO. 13) (See Figure 11)	0.4	2.9	3
GFB-133	"	3-GDGY (SEQ ID NO. 6)-1-CO_2H (See Figure 11)	0.8	3.2	3
GFB-134	"	3-GDGY (SEQ ID NO. 6)-1-GDDY (SEQ ID NO. 14) (See Figure 11)	1.9	2.5	2.6
GFB-135	"	3-GDGY (SEQ ID NO. 6)-1-GDDD (SEQ ID NO. 2) (See Figure 11)	1.9	3.2	24

GFB-136	"	3-GDDD (SEQ ID NO. 2)-1-GDGY (SEQ ID NO. 6) (See Figure 11)[	3	25	24
GFB-137	"	2-GDGY (SEQ ID NO. 6)-1-GDDG (SEQ ID NO. 13) (See Figure 11)	0.4	2.9	47

Page 21, line 6:

[1]GFB-108: The "d" refers to D-amino aicd, so-ADGD is (D-Ala)-Asp-Gly-Asp (SEQ ID NO. 3).

Page 27, line 19:

In order to identify molecules that would bind vascular endothelial growth factor (VEGF), Flk-1/3T3 cell-based assay is used that relies on VEGF-stimulation of its receptor, Flk-1, tyrosine phosphorylation and subsequent MAP-kinase activation. The assay used herein identical to that used for PDGF, except that NIH 3T3 cells that overexpress Flk-1 are used. GFB-116, which has four identical loops with the sequence GKGK (SEQ ID NO. 10) is shown to be very potent and selective toward blocking the ability of VEGF to stimulate Flk-1 tyrosine phosphorylation and subsequent MAP-kinase activation as measured by phospho erk-1 and erk-2 also referred to in the Table as p42 and p44 (Table 4A). A preferred embodiment of the invention is a compound that binds to a vascular endothelial growth factor, of the general structure III (above) in which R is n-butyl, n-propyl, or benzyl, and X comprise covalently attached identical cyclic peptide loops wherein R_1, R_2, R_3, and R_4 are each amino acid side chains, as broadly defined above, that define a tetrapeptide sequence, wherein said tetrapeptide is covalently attached at the amino and carboxy termini of said tetrapeptide to 3-aminomethyl-5aminobenzamide linking group, and wherein said tetrapeptide sequence is GKGK (SEQ ID NO. 10), GDGY (SEQ ID NO. 6), or functionally related derivatives thereof.

Pages 28 and 29, Table 4B:

Table 4B. Inhibition of VEGF stimulated Flk-1 Tyrosine Phosphorylation and Signaling in Flk-1/3T3 by GFBs.

Designation	Scaffold	R_1-R_4 sequence	(IC_{50}) Inhibition (μM)		
			Flk-1-Y-P	p42	p44
GFB-101	O4-Calix[A]	4-GFGD (SEQ ID NO. 15)	>100	>100	>100
GFB-102	"	4-GDFD (SEQ ID NO. 1)	100	>100	>100
GFB-103	"	4-GDGD (SEQ ID NO. 16)			
GFB-104	O3-Calix[A]	4-GDGD (SEQ ID NO. 16)			
GFB-105	But-Calix[A]	4-GDFD (SEQ ID NO. 1)	<10	>100	>100
GFB-106	"	4-GDDD (SEQ ID NO. 2)	<10	<10	<10
GFB-107	"	4-GDGD (SEQ ID NO. 16)	<10	100	100
GFB-108	"	4-d-ADGD[1] (SEQ ID NO. 3)	10	50	50
GFB-109	"	4-GDLD (SEQ ID NO. 4)			
GFB-110	"	4-GDAD (SEQ ID NO. 5)			
GFB-111	"	4-GDGY (SEQ ID NO. 6)	5	10	10
GFB-112	"	4-ADGD (SEQ ID NO. 7)	<10	10	10
GFB-113	"	4-GDSD (SEQ ID NO. 8)	<10	10	10
GFB-114	"	(4-) 8-acid (See Figure 7)			
GFB-115		4-GKGF (SEQ ID NO. 9)		5 10	5 10
GFB-116		4-GKGK (SEQ ID NO. 10)	0.3	5	5
GFB-117		4-GDND (SEQ ID NO. 11)			

GFB-118		4-D-2-NalDGD[2] (SEQ ID NO. 17)			
GFB-119		4-PDGD (SEQ ID NO. 12)			
GFB-120	"	4-GDDG (SEQ ID NO. 13)			
GFB-121	"	4-d-AbuDGD[3] (SEQ ID NO. 18)			
GFB-122	"	4-GDDY (SEQ ID NO. 14)			
GFB-123	"	1-GDDG (SEQ ID NO. 13)			
GFB-124	"	See Figure 8			
GFB-126	"	3 x GDDG (See Figure 9) (SEQ ID NO. 13)			
GFB-127	"	2 x GDDG (See Figure 9) (SEQ ID NO. 13)			
GFB-128	"	DPM-2-GDGY (See Figure 10) (SEQ ID NO. 6)			
GFB-129	"	DPM-2-GDDD (See Figure 10) (SEQ ID NO. 2)			
GFB-130	"	DPM-2-GDDY (See Figure 10) (SEQ ID NO. 14)			
GFB-131	"	DPM-2-GDDG (See Figure 10) (SEQ ID NO. 13)			
GFB-132	But-Calix	3-GDGY (SEQ ID NO. 6)-1-GDDG (SEQ ID NO. 13) (See Figure 11)			
GFB-133	"	3-GDGY (SEQ ID NO. 6)-1-CO_2H (See Figure 11)			

GFB-134	"	3-GDGY (SEQ ID NO. 6)-1-GDDY (SEQ ID NO. 14) (See Figure 11)			
GFB-135	"	3-GDGY (SEQ ID NO. 6)-1-GDDD (SEQ ID NO. 2) (See Figure 11)			
GFB-136	"	3-GDDD (SEQ ID NO. 2)-1-GDGY (SEQ ID NO. 6) (See Figure 11)[			
GFB-137	"	2-GDGY (SEQ ID NO. 6)-1-GDDG (SEQ ID NO. 13) (See Figure 11)			

Page 30, line 4:

[1]GFB-108: The "d" refers to D-amino acid, so d-ADGD is (D-Ala)-Asp-Gly-Asp SEQ ID NO. 3).

Page 31 and 32, Table 5:

Table 5. Inhibition of aFGF stimulated FGFR Tyrosine Phosphorylation and Signaling in NIH 3T3 by GFBs.

Designation	Scaffold	R_1-R_4 sequence	(IC_{50}) Inhibition (μM) FGFR-Y-P p42 p44
GFB-101	O4-Calix[A]	4-GFGD (SEQ ID NO. 15)	ND
GFB-102	"	4-GDFD (SEQ ID NO. 1)	ND

GFB-103	"	4-GDGD (SEQ ID NO. 16)	ND		
GFB-104	O3-Calix[A]	4-GDGD (SEQ ID NO. 16)	ND	2.5	0.7
GFB-105	But-Calix[A]	4-GDFD (SEQ ID NO. 1)	ND	66.4	75.7
GFB-106	"	4-GDDD (SEQ ID NO. 2)	ND	95.1	98.2
GFB-107	"	4-GDGD (SEQ ID NO. 16)	ND	57.3	59.7
GFB-108	"	4-d-ADGD[1] (SEQ ID NO. 3)	ND	67.8	80.1
GFB-109	"	4-GDLD (SEQ ID NO. 4)	ND	68.3	79.7
GFB-110	"	4-GDAD (SEQ ID NO. 5)	ND	76.1 93.0	85.2 98.9
GFB-111	"	4-GDGY (SEQ ID NO. 6)	ND	51.0 39.0	68.0 51.8
GFB-112	"	4-ADGD (SEQ ID NO. 7)	ND	59.7 40.2	62.9 39.6
GFB-113	"	4-GDSD (SEQ ID NO. 8)	ND	53.6	64.3
GFB-114	"	(4-) 8-acid (See Figure 7)	ND	-8.7	-16.9
GFB-115		4-GKGF (SEQ ID NO. 9)	ND	-21.0	-23.9
GFB-116		4-GKGK (SEQ ID NO. 10)	ND	99.2 99.6 101.9 99.7 **100.1±1.2**	97.5 97.2 116.2 99.9 **102.7±9.1**

GFB-117		4-GDND (SEQ ID NO. 11)	ND	63.4 67.6	80.8 84.3
GFB-118		4-D-2-NalDGD[2] (SEQ ID NO. 17)	ND	20.6	30.5
GFB-119		4-PDGD (SEQ ID NO. 12)	ND	62.6 72.1 47.8 **60.8±12.2**	78.9 81.7 58.1 **72.9±12.9**
GFB-120	"	4-GDDG (SEQ ID NO. 13)	ND	68.1	74.3
GFB-121	"	4-d-AbuDGD[3] (SEQ ID NO. 18)	ND	8.7	8.9
GFB-122	"	4-GDDY (SEQ ID NO. 14)	ND	57.3	71.6
GFB-123	"	1-GDDG (SEQ ID NO. 13)	ND	11.4	12.5
GFB-124	"	See Figure 8	ND	0.3	-1.7
GFB-126	"	3 x GDDG (See Figure 9) (SEQ ID NO. 13)	ND	96.5	106.0
GFB-127	"	2 x GDDG (See Figure 9) (SEQ ID NO. 13)	ND	97.5	107.4
GFB-128	"	DPM-2-GDGY (See Figure 10) (SEQ ID NO. 6)	ND	23.5	43.3

GFB-129	"	DPM-2-GDDD (See Figure 10) (SEQ ID NO. 2)	ND	11.3	3.2
GFB-130	"	DPM-2-GDDY (See Figure 10) (SEQ ID NO. 14)	ND	78.9	78.9
GFB-131	"	DPM-2-GDDG (See Figure 10) (SEQ ID NO. 13)	ND	33.4	44.1
GFB-132	But-Calix	3-GDGY (SEQ ID NO. 6)-1-GDDG (SEQ ID NO. 13) (See Figure 11)	ND	48.2	50.2
GFB-133	"	3-GDGY (SEQ ID NO. 6)-1-CO_2H (See Figure 11)	ND	95.8	101.0
GFB-134	"	3-GDGY (SEQ ID NO. 6)-1-GDDY (SEQ ID NO. 14) (See Figure 11)	ND	54.8	64.1
GFB-135	"	3-GDGY (SEQ ID NO. 6)-1-GDDD (SEQ ID NO. 2) (See Figure 11)	ND	44.1	53.9
GFB-136	"	3-GDDD (SEQ ID NO. 2)-1-GDGY (SEQ ID NO. 6) (See Figure 11)[	ND	73.1	84.5
GFB-137	"	2-GDGY (SEQ ID NO. 6)-1-GDDG (SEQ ID NO. 13) (See Figure 11)	ND	6.4	19.9

Page 32, line 6:

[1]GFB-108: The "d" refers to D-amino acid, so d-ADGD is (D-Ala)-Asp-Gly-Asp (SEQ ID NO. 3).

Page 33 and 34, Table 6:

Table 6. Inhibition of IGF-1 stimulated IGFR Tyrosine Phosphorylation and Signaling in IGFR/ 3T3 by GFBs.

Designation	Scaffold	R_1-R_4 sequence	% Inhibition at 100μM IGF1R-Y-P	p42	p44
GFB-101	O4-Calix[A]	4-GFGD (SEQ ID NO. 15)	ND		
GFB-102	"	4-GDFD (SEQ ID NO. 1)	ND		
GFB-103	"	4-GDGD (SEQ ID NO. 16)	ND		
GFB-104	O3-Calix[A]	4-GDGD (SEQ ID NO. 16)	-28.4	-0.19	22.4
GFB-105	But-Calix[A]	4-GDFD (SEQ ID NO. 1)	1.3		
GFB-106	"	4-GDDD (SEQ ID NO. 2)	ND		
GFB-107	"	4-GDGD (SEQ ID NO. 16)	ND	57.3	59.7
GFB-108	"	4-d-ADGD[1] (SEQ ID NO. 3)	ND	67.8	80.1
GFB-109	"	4-GDLD (SEQ ID NO. 4)	ND	68.3	79.7
GFB-110	"	4-GDAD (SEQ ID NO. 5)	40.9 32.4	27.2 8.6	55.4 47.1
GFB-111	"	4-GDGY (SEQ ID NO. 6)	-12.4	-18.4	10.7

GFB-112	"	4-ADGD (SEQ ID NO. 7)	0.6	-7.6	30.4
GFB-113	"	4-GDSD (SEQ ID NO. 8)	-18.9	-31.4	18.7
GFB-114	"	(4-) 8-acid (See Figure 7)	-28.9	43.6	76.8
GFB-115		4-GKGF (SEQ ID NO. 9)	-38.3	-12.4	51.9
GFB-116		4-GKGK (SEQ ID NO. 10)	-149.2 -90.0	-29.8 5.2	25.2 43.5
GFB-117		4-GDND (SEQ ID NO. 11)	4.9	17.1	61.5
GFB-118		4-D-2-NalDGD[2] (SEQ ID NO. 17)	1.5	16.4	55.2
GFB-119		4-PDGD (SEQ ID NO. 12)	16.7	29.7	66.2
GFB-120	"	4-GDDG (SEQ ID NO. 13)	35.4	68.1	85.9
GFB-121	"	4-d-AbuDGD[3] (SEQ ID NO. 18)	33.8	28.3	62.1
GFB-122	"	4-GDDY (SEQ ID NO. 14)	38.4	33.6	66.6
GFB-123	"	1-GDDG (SEQ ID NO. 13)	24.2	26.7	62.4
GFB-124	"	See Figure 8	-9.5	3.0	-20.4
GFB-126	"	3 x GDDG (See Figure 9) (SEQ ID NO. 13)	51.7 51.0	63.9 47.0	71.2 79.2
GFB-127	"	2 x GDDG (See Figure 9) (SEQ ID NO. 13)	36.8 31.8	38.4 27.2	61.6 74.4

GFB-128	"	DPM-2-GDGY (See Figure 10) (SEQ ID NO. 6)	-12.0	-6.1	38.2
GFB-129	"	DPM-2-GDDD (See Figure 10) (SEQ ID NO. 2)	3.4	2.8	33.4
GFB-130	"	DPM-2-GDDY (See Figure 10) (SEQ ID NO. 14)	22.7	-19.7	-17.5
GFB-131	"	DPM-2-GDDG (See Figure 10) (SEQ ID NO. 13)	30.2	-6.2	20.0
GFB-132	But-Calix	3-GDGY (SEQ ID NO. 6)-1-GDDG (SEQ ID NO. 13) (See Figure 11)	30.2	11.0	39.4
GFB-133	"	3-GDGY (SEQ ID NO. 6)-1-CO_2H (See Figure 11)	ND	ND	ND
GFB-134	"	3-GDGY (SEQ ID NO. 6)-1-GDDY (SEQ ID NO. 14) (See Figure 11)	16.8	4.9	53.5
GFB-135	"	3-GDGY (SEQ ID NO. 6)-1-GDDD (SEQ ID NO. 2) (See Figure 11)	16.2	0.8	46.1
GFB-136	"	3-GDDD (SEQ ID NO. 2)-1-GDGY (SEQ ID NO. 6) (See Figure 11)[	40.6	15.0	59.559.5

GFB-137	"	2-GDGY (SEQ ID NO. 6)-1-GDDG (SEQ ID NO. 13) (See Figure 11)	36.0	5.9	38.2

Page 34, line 6:

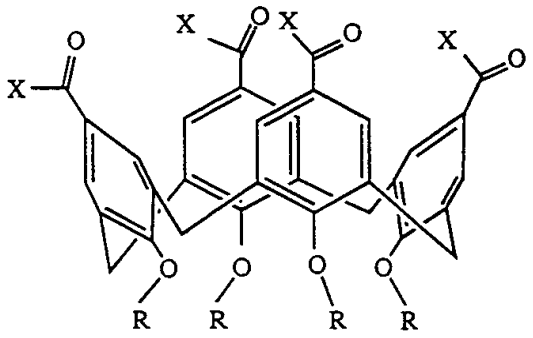
[1]GFB-108: The "d" refers to D-amino acid, so d-ADGD is (D-Ala)-Asp-Gly-Asp (SEQ ID NO. 3).

Marked-Up Version of Amended Claims:

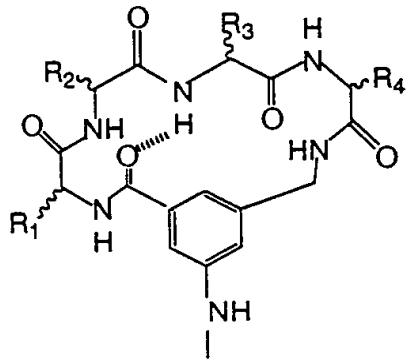
Please substitute the following claims:

Claim 4 (amended):

A growth factor binding compound, of the general structure:



wherein R is n-butyl, n-propyl, benzyl, (C_1-C_{12}) alkyl, (C_7-C_{18}) aralkyl, (C_6-C_{18}) aryl, (C_1-C_{12}) alkenyl, (C_7-C_{18}) aralkenyl, (C_1-C_{12}) alkylether, and X are independently cyclic peptide loops of the general structure:



wherein R_1, R_2, R_3, and R_4 are each amino acid side chains that define a tetrapeptide sequence, wherein said tetrapeptide is covalently attached at the amino and carboxy termini of said tetrapeptide to a 3-aminomethyl-5-aminobenzamide linking group, and wherein said tetrapeptide sequence is selected from the group consisting of GDFD (SEQ ID NO. 1), GDDD (SEQ ID NO. 2), D-ADGD (SEQ ID NO. 3), GDLD (SEQ ID NO. 4), GDAD (SEQ ID NO. 5), GDGY (SEQ ID NO. 6),

ADGD (SEQ ID NO. 7), GDSD (SEQ ID NO. 8), GKGF (SEQ ID NO. 9), GKGK (SEQ ID NO. 10), GDND (SEQ ID NO. 11), PDGD (SEQ ID NO. 12), GDDG (SEQ ID NO. 13), and GDDY (SEQ ID NO. 14).

Claim 5 (amended):

The compound of claim 4, in which said growth factor is a platelet derived growth factor, and wherein said tetrapeptide sequence is GDGY (SEQ ID NO. 6).

Claim 15 (amended):

The compound of claim 1 wherein said growth factor is vascular endothelial growth factor and wherein said tetrapeptide sequence is GKGK (SEQ ID NO. 10), GDGY , or functionally related derivatives thereof.

Claim 16 (amended):

The compound of claim wherein said growth factor is acidic fibroblast growth factor and wherein said tetrapeptide sequence is GDDD (SEQ ID NO. 2), GKGK (SEQ ID NO. 10), GDDG (SEQ ID NO. 13), GDGY (SEQ ID NO. 6), or functionally related derivatives thereof.

Claim 17 (amended):

The compound of claim 1 wherein said growth factor is insulin-like growth factor-1 and wherein said tetrapeptide sequence is GDDG (SEQ ID NO. 13) or functionally related derivatives thereof.